PHARMACEUTICAL COMPOSITION IN CAPSULES THAT COMPRISES A NON-STEROIDAL ANTIINFLAMATORY AND AN OPIATE ANALGESIC FOR HANDLING PAIN

FIELD OF THE INVENTION

The present invention is referred as the association or combination of a non-steroidal anti-inflammatory agent such as ketorolac and an opiate analgesic known as tramadol; which are formulated into capsules and that are given to patients who have pain.

The combination of these substances, gives as a result a greater analgesic effect, with an analgesic synergy, as opposed to when these substances are independently administered. The dosage is also less, avoiding side effects when other methods of administration are used or when they are independently used.

BACKGROUND OF THE INVENTION

Ketorolac is a non-steroidal anti-inflammatory agent with analgesic properties. In the case of pain, it can be administered orally or by injection (intramuscularly or intravenously). It has been shown that Ketorolaco shows an analgesic efficiency comparable

with opiates, according to clinical studies reported by Yee *et al* in 1986; O'Hara *et al* in 1987, and Forbes *et al* in 1990.

It has been shown that Ketorolac acts over the ciclo-oxygenase enzyme, which acts on the pain and inflammatory process, it has a plasmatic half-life of 4 to 6 hours. About 90% of the dose is excreted through the urine without changes; the rest is excreted through the feces.

Tramadol is an opiate analgesic, it has noradrenergic and serotoinergic properties that contribute in its analgesic activities. It is used to moderate severe pain. It can be administered orally, intramuscularly or intravenously. Tramadol half-life is 6 hours and is mainly excreted through the urine.

Our interest was to create a combination of a non-steroidal anti-inflammatory with analgesic activity as ketorolac and of an opiate analgesic such as tramadol, with less dosage, to be administered orally, avoiding the typical side effects when administered independently and with greater dosage.

There was an unexpected side effect between the two active agents administered

together, differently than those obtained when administered independently, furthermore we also used less dosage without side effects.

DETAILED DESCRIPTION OF THE INVENTION

In the last couple of years has increased the associative research between analgesic medicines, with the objective of create an analgesic synergy, using less dosage and reducing the side effects of those obtained when administered independently, using greater dosages.

A clinical study was performed, using the combination of ketorolac/tramadol capsules in 100 patients suffering postoperative pain because the second molar extraction.

The patients fulfilled a questionnaire, with the objective of determining the efficacy of the ketorolac/tramadol combination. A visual analog scale (VAS) was applied to them to measure the pain intensity, before and after the administration of the combination, the initiation time was measured until 15 and 30 minutes after administration and side effects were observed.

The results are the following:

Table 1:

MEASUREMENT OF PAIN BEFORE ADMINISTRATION

Symptoms	No. OF PATIENTS
Pain	
Absent	0
Low	25
Moderate	50
Severe	25

Table 2

MEASUREMENT OF PAIN 15 MINUTES AFTER ADMINISTRATION

SYMPTOMS	No. of Patients
Pain	
Absent	75
Low	20
Moderate	5
Severe	0

Table 3

MEASUREMENT OF PAIN 30 MINUTES AFTER ADMINISTRATION

Symptoms	No. of Patients
Pain	
Absent	80
Low	18
Moderate	2
Severe	0

Side effects were not reported during and after the administration.

MEASUREMENT OF PAIN 45 MINUTES AFTER ADMINISTRATION

Symptoms	No. of Patients
Pain	
Low	81
Moderate	19
Severe	0

Side effects were not reported during and after the administration

Composition:

Ketorolaco Tromethamine .....from 0.0010 g to 0.10000 g

Tramadol hydrochloride .....from 0.0001 g to 0.20000 g

Colloidal silicon dioxide..... from 0.0001 g to 0.20000 g

Sodium glicolate starch.....from 0.010 g to 0.20000 g

Lactose .....from 0.0100 g to 0.50000 g

Microcrystalline cellulose.....from 0.0100 g to 0.5000 g

Magnesium estearate .....from 0.0001g to 0.02000 g

Excipients.....from 0.0001 g to 1.0000 g

Elaboration process

1. Mix the ketorolac tromethanine, the colloidal silicate dioxide, the tramadol hydrochloride, sodium glicolate starch, the lactose, the microcrystalline cellulose, the magnesium stearate and other recipients if necessary
2. Analyze the powdered mix
3. Proceed to encapsuling and conditioning

It is important to notice that the combination of the active principles stated above offer great advantages, differently than those obtained when administered independently. In the combination of said

principles the dose is less and the efficacy is excellent. This combination results in a reduction of side effects of those obtained when the active principles are administered independently and in greater doses.